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LISTING OF THE CLAIMS

Claim 1 (canceled)

Claim 2 (currently amended) A method for the production of a single heavy chain antibody in a transgenic non-human mammal comprising expressing a heterologous VHH heavy chain locus in that mammal specifically in B cells in response to antigen challenge wherein the VHH heavy chain locus is integrated into the non-human mammal's genome and said VHH heavy chain locus comprises:

- (a) at least one VHH exon, at least one D exon and at least one J exon, wherein the VHH exon, the D exon and the J exon are capable of recombining to form a VDJ coding sequence, and wherein the VHH exon comprises a naturally occurring VHH coding sequence, and
- (b) a constant heavy chain region comprising at least one constant heavy chain gene, wherein each of said at least one constant heavy chain gene, when expressed, does not express a functional CH1 domain.
- (c) a locus control region (LCR) providing for expression of the VHH heavy chain locus specifically in B cells

said method comprising:

- 1) immunizing said mammal with an antigen and
- 2) isolating single heavy chain antibody against said antigen.

Claims 3-6 (canceled)

Claim 7 (currently amended) The method of claim 2 or 41 wherein the VHH single heavy chain locus comprises a camelid VHH, at least one D exon of human origin, [[and]] at - 3 -

least one J exon of human origin, and a constant region of human origin.

Claims 8 - 9 (canceled)

Claim 10 (previously presented) The method of claim 2 or 41 wherein the constant heavy chain region comprises at least one constant region heavy chain gene which is of noncamelid origin.

Claim 11 (previously presented) The method of claim 10 wherein at least one constant region heavy chain gene is of human origin.

Claims 12 – 32 (canceled)

Claim 33 (previously presented) The method of claim 2 or 41 wherein the entire VHH single heavy chain locus is of camelid origin

Claims 34-38 (canceled)

Claim 39 (previously presented) The method according to claim 2 or 41 wherein the non-human mammal is a rodent.

Claim 40 (canceled)

Claim 41 (currently amended) A method for the production of a single heavy chain antibody in a transgenic mouse comprising expressing a heterologous VHH heavy chain locus in the mouse specifically in B cells in response to antigen challenge wherein the VHH heavy chain locus in integrated into said mouse's genome and said VHH heavy chain locus comprises:

(a) at least one VHH exon, at least one[[-D]] <u>D</u> exon and at least one[[-J]] <u>J</u> exon, wherein the VHH exon, the D exon and the J exon are capable of recombining to form <u>a</u> VDJ coding sequence, and wherein the VHH exon comprises a naturally occurring VHH coding sequence.

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and

- (b) a constant heavy chain region comprising at least one constant heavy chain gene, wherein each of said at least one constant heavy chain gene, when expressed, does not express a functional CH1 domain.
- (c) a regulatory sequence providing for expression of the VHH heavy chain locus specifically in B cells

said method comprising:

- 1) immunizing said mammal with an antigen and
- 2) isolating single heavy chain antibody against said antigen,

Claim 42 (canceled)

Claim 43 (previously presented) The method of claim 2 or 41 wherein said antibody is isolated using hybridoma technology.

Claim 44 (previously presented) The method of claim 2 or 41 wherein said antibody comprises a variable region fragment and said variable region fragment is isolated using phage display.